

Declaration of Jeffery S. Carter Under 37 C.F.R. 1.132

I, Jeffery S. Carter, Ph.D., declare and state as follows:

1. I am currently employed by Pfizer Corporation.
2. I am a co-inventor of the subject matter claimed in U.S. Patent Application Serial No. 09/496,695 filed February 2, 2000, entitled "Substituted Benzopyran derivatives for the Treatment of Inflammation."

3. Together with my co-inventors we synthesized and tested numerous chromene compounds having formula I as detailed in my Application. In the course of preparing my application, several compounds were tested for COX-1 and COX-2 inhibitory activity as detailed in the "biological evaluation" section of the application. Results from the assay were expressed as IC₅₀ values. By way of example, three different chromene compounds of formula I, each having a positional isomer were tested. As detailed in Exhibit 1, IC₅₀ values were compared between two positional isomeric forms of each of three sets of chromenes of formula I (i.e., SC-74057 and SC-71277; SC-71198 and PHA-00737581; SC-77158 and SC-75783). The positional isomers of each set had significantly different IC₅₀ values.

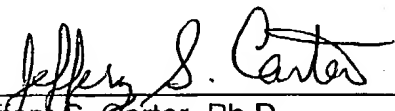
In the first pair of positional isomers, the COX-1 and COX-2 IC₅₀s were compared and were found to be significantly different from one another. The COX-2 IC₅₀ value for SC-71198 was >100 μ M while the COX-2 IC₅₀ value for a corresponding positional isomer of the compound (PHA-00737581) was 0.15 μ M. The COX-1 IC₅₀ value for SC-71198 was >100 μ M while the COX-1 IC₅₀ value for a corresponding positional isomer of the compound (SC-71277) was 24.4 μ M.

In the second pair of positional isomers, the COX-1 and COX-2 IC₅₀s were also markedly different from one another. The COX-2 IC₅₀ value for SC-77158 was >100 μ M while the COX-2 IC₅₀ value for a corresponding positional isomer of the compound (SC-75783) was 0.188 μ M. The COX-1 IC₅₀ value for SC-77158 was >100 μ M while the COX-1 IC₅₀ value for a corresponding positional isomer of the compound (SC-75783) was 4.78 μ M.

In the third set, the COX 1 and COX 2 IC₅₀ values of positional isomers SC-74057 and SC-71277 were compared and were also found to be significantly different from one another. The COX-2 IC₅₀ value for SC-74057 was >500 μ M while the COX-2 IC₅₀ value for a corresponding positional isomer of the compound (SC-71277) was 35 μ M. Similarly, the COX-1 IC₅₀ value for SC-74057 was >500 μ M while the COX-1 IC₅₀ value for a corresponding positional isomer of the compound (SC-71277) was 61 μ M.

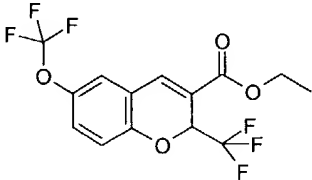
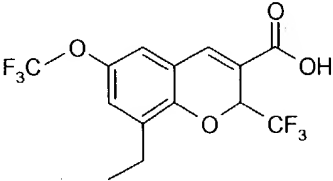
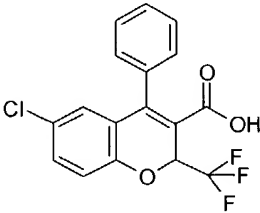
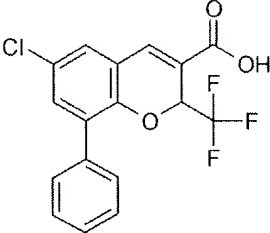
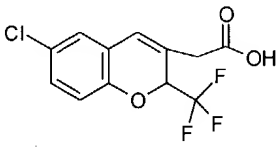
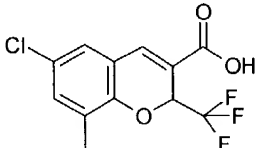
A copy of Table 1 is attached to this Declaration as Exhibit 1.

4. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.


Jeffery S. Carter, Ph.D.

02-06-04

Date

		hCox-2	hCox-1
Compound No.	Structure	IC50 (uM)	IC50 (uM)
SC-71198		>100	>100
PHA-00737581		0.15	24.4
SC-77158		>100	>100
SC-75783		0.188	4.78
SC-74057		>500	>500
SC-71277		35	61